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(54) Title: METHODS FOR MONITORING PROTEASE INHIBITOR ANTIRETROVIRAL THERAPY

(57) Abstract: This invention relates to antiviral drug susceptibility and resistance tests to be used in idregimens for the treatment of human immunodeficiency virus (HIV) infection and acquired immunodeficiency virus (HIV) infection acquired immunode

(57) Abstract: This invention relates to antiviral drug susceptibility and resistance tests to be used in identifying effective drug regimens for the treatment of human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS), particularly treatment regimes including a protease inhibitor. The invention further relates to the means and methods of monitoring the clinical progression of HIV infection and its response to antiretroviral therapy using phenotypic or genotypic susceptibility assays.



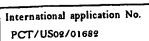




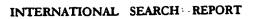
International application No. PCT/US02/01682

A. CLASSIFICATION OF SUBJECT MATTER 1PC(7) :C12N 9/00, 9/50; C12Q 1/57 US CL :495/23, 183, 219 According to International Patent Classification (IPC) or to b B. FIELDS SEARCHED				
Minimum documentation searched (classification system followed by classification symbols) U.S.: 485/25, 183, 219				
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched				
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) BIOSIS, MEDLINE, WEST				
C. DOCUMENTS CONSIDERED TO BE RELEVANT				
Category Citation of document, with indication, where	appropriate, of the relevant passages	Relevant to claim No.		
Y US 5,837,464 A (CAPON et al) 1 document.	7 November 1998, see entire	1-6, 10-16 and 20- 23		
YOUNG, B. et al. Resistance Mut Transcriptase Genes of Human Im Isolates from Patients with Comb Failure. Journal of Infectious Diseas No. 5, pages 1497-1501, see entire	munodeficiency Virus Type 1 ination Antiretroviral Therapy ses. November 1998, Vol. 178,	1-6, 10-16 and 20- 23		
X Further documents are listed in the continuation of B Special categories of cited documents: "A" document defining the general state of the art which is not consider to be of particular relevance "E" earlier document published on or after the international filing dates.	"I" later document published after the in date and nut in conflict with the ap the principle or theory underlying the document of particular relevance; to considered novel or cannot be considered novel or cannot be document in taken admin	"I" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step		
"L" document which may three doubts on priority claim(s) or which cited to establish the publication date of another citation or off special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or off means "P" document published prior to the international filing date but ha	nor "Y" document of particular relevance; to considered to involve an inventive ste with one or more other such doct obvious to a person skilled in the ar	p when the document is computed ments, such combination being t		
Date of the actual completion of the international search 16 JUNE 2002	0 9 JUL 2002	Date of mailing of the international search report		
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230 Authorized officer LAURIE SCHEINER Telephone No. (705) 808-0196				



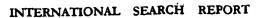


C (Continua	tion). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Cab relevant marcages		Relevant to claim No.
Y	HERIOGS et al A Rapid Method for Simultaneous Detection of 1-		1-6, 10-16 and 20-23
		Λ.	



International application No.
PCT/US02/01682

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)		
This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:		
1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:		
2. Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:		
5. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).		
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)		
This International Searching Authority found multiple inventions in this international application, as follows:		
Please See Extra Sheet.		
<i>:</i>		
1. As all required additional search fees were timely paid by the applicant, this international search report covers a searchable claims.		
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.		
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:		
4. X No required additional search fees were timely paid by the applicant. Consequently, this international search report restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-6, 10-16 and 20-23 (in-part)		
Remark on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.		





International application No. PCT/US02/01682

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 15.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group 1, claim(s) 1-6, 10-16, 20-25, drawn to a method of by evaluating whether a sample contains a mutation at code 32.

Group II, claim(s) 1-23, drawn to a method of assessing the effectiveness of protease antiretroviral therapy by evaluating whether a sample contains a mutation at codon 90.

Group III, claim(s) 24 and 25, drawn to a resistance test vector encoding a protease with a mutation at codon 82. Group IV, claims 24 and 25, drawn to a resistance test vector encoding a protease with a mutation at codon 90.

The inventions listed as Groups I-IV do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Claim 1 is drawn to a method of assessing the effectiveness of antiretroviral therapy in an HIV-infected patient by evaluating whether a biological sample from the patient has a mutation at codon 82 and a secondary mutation and determining the change in susceptibility to a protease inhibitor. Lorenzi et al. (AIDS. 1997; 11 (12): F95-9, abstract only) teaches collecting samples from HIV-infected patients, sequencing the protease gene after drug therapy, and determining that non-responders developed mutations at codons 82 and 48, which confers resistance to antiviral drugs. Since neither the instant method steps nor the claimed mutations are novel in the art, it is determined that the instant claims lack unity of invention.

Group II is drawn to a second method of evaluating distinct mutations from group I.

Group III is drawn to a first product.

Group IV is drawn to a second product.